

Musical Hallucinations in Patients with Lyme Disease

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Abstract: Musical hallucinations are poorly understood auditory hallucinations that occur in patients with otologic or neurologic diseases. We report the first cases of musical hallucinations in two patients with neurologic Lyme disease. Both subjects were women with clinical and laboratory evidence of chronic Lyme disease, progressive neurologic dysfunction, and abnormal magnetic resonance imaging of the brain. There was no evidence of hearing loss in either case. Musical hallucinations had a sudden onset and took the form of patriotic or operatic music. The auditory hallucinations disappeared with intravenous (IV) antibiotic therapy in both patients, but the hallucinations recurred when IV antibiotic therapy was discontinued in one case. Response to therapy was accompanied by an increase in the CD57 lymphocyte subset in one patient, whereas recurrent hallucinations were associated with persistently low CD57 levels in the other case. We conclude that musical hallucinations may be associated with neurologic Lyme disease. These auditory hallucinations appear to respond to IV antibiotic therapy. Patients with musical hallucinations of unknown cause should be tested for infection with the Lyme disease spirochete.

Key Words: CD57 lymphocytes, Lyme disease, musical hallucinations, neuroborreliosis

Musical hallucinations are a rare form of complex auditory hallucinations characterized by repetitive and usually uncontrollable musical patterns that are unrelated to external stimuli.^{1,2} Musical hallucinations have been associated with infectious agents, neurologic disease, psychiatric illness, and various medications.¹⁻⁸ Although visual and vocal hallucinations have been reported in patients with Lyme disease,^{9,10} musical hallucinations have not previously been described as a neurologic complication of this disorder. We

report the first cases of musical hallucinations in patients with neurologic Lyme disease.

Case Reports

Patient 1

Patient 1 was a 66-year-old woman with a 7-year history of Lyme disease, which was diagnosed on the basis of a tick bite, presence of an erythema migrans rash, and positive serology (enzyme-linked immunosorbent assay and Western blot) for the spirochete *Borrelia burgdorferi*. At the time of infection, the patient was living in Sonoma County, California. Over the years, she had suffered from recurrent musculoskeletal and flu-like symptoms, and she had been treated with various oral antibiotics including doxycycline, amoxicillin, clarithromycin, and azithromycin. She took aspirin intermittently for pain, and she had taken a stable dose of estrogen since menopause. She did not smoke and she drank alcohol occasionally. Recently, she had developed progressive fatigue, short-term memory loss, and logamnesia. Physical examination was unremarkable, and neurologic testing confirmed poor object recall and word searching. Cerebrospinal fluid analysis yielded a positive test for *B. burgdorferi* by polymerase chain reaction. Brain magnetic resonance imaging (MRI) revealed multiple bilateral white

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Key Points

- Musical hallucinations occur in patients with chronic Lyme disease.
- The auditory hallucinations may have an abrupt onset, and they appear to respond to intravenous antibiotic therapy.
- In chronic Lyme disease, these hallucinations may be associated with right temporal lobe lesions and decreased CD57 natural killer cell levels.
- Patients with musical hallucinations should be screened for infection with the Lyme disease spirochete.

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Accepted August 2, 2002.

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0038-4348/03/9607-0711

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matter lesions consistent with neurologic Lyme disease. Rapid plasma reagin testing was negative.

The patient initially refused intravenous (IV) antibiotic therapy, and she was retreated with clarithromycin and amoxicillin. However, after 4 weeks of this treatment she noted the sudden onset of musical hallucinations characterized by repetitive playing of "The Star-Spangled Banner." The music was bilateral, constant, and woke her at night. She stated that one of her earliest childhood memories was hearing patriotic music, which she did not enjoy as an adult. Tinnitus was absent, and auditory testing (tone conduction and speech discrimination) was normal. An electroencephalogram was normal.

She was treated with IV ceftriaxone and her musical hallucinations resolved completely over 4 weeks. However, her memory loss and logamnesia persisted, and she continued on IV antibiotic treatment for 9 months. The neurologic symptoms gradually resolved, and she discontinued antibiotic therapy. A single-photon emission computed tomographic (SPECT) brain scan performed after 8 months of IV antibiotic therapy was negative for perfusion defects. The musical hallucinations have not recurred during 6 months of follow-up. The patient's CD57 lymphocyte level was initially normal on oral antibiotics, and the level increased on IV antibiotic therapy (Fig. 1).

Patient 2

Patient 2 was an 80-year-old woman who was bitten by a tick and developed a "bull's-eye" rash 4 years previously while living in Santa Cruz County, California. She did not seek medical attention, and she remained in good health. She had been treated with stable doses of atorvastatin and thyroxine for years. Over the past 2 years, she had developed clumsiness, balance problems, short-term memory loss, and fatigue. She also noted a hand tremor for the past month. She did not smoke or drink alcohol. A son who lived nearby had recently been diagnosed with Lyme

disease. Physical examination revealed an intention tremor and cogwheel rigidity in the upper extremities. A serologic test (Western blot analysis) for *B. burgdorferi* was strongly positive. Thyroid function tests were normal, and rapid plasma reagin testing was negative. The patient refused lumbar puncture. Brain MRI revealed multiple periventricular white matter lesions and mild cortical atrophy.

She was treated with oral doxycycline and her tremor and rigidity disappeared. However, her short-term memory loss persisted, and after 2 months of antibiotic treatment she noted the abrupt onset of musical hallucinations in the form of repetitive playing of Italian opera. The music was constant and louder at night. She stated that one of her earliest childhood memories was hearing Italian opera played by her parents, and although she did not enjoy the music she said that the memory was a pleasant one. Tinnitus was absent, and auditory testing (tone conduction and speech discrimination) was normal for the patient's age.

The patient initially refused IV antibiotics, but she continued the doxycycline. The musical hallucinations and memory problems persisted. After 6 months of oral antibiotics, she consented to treatment with IV ceftriaxone. Within 3 weeks, the musical hallucinations had disappeared and her memory had improved. However, after 2 months of IV therapy, she had increased liver function tests and cholelithiasis. IV ceftriaxone was discontinued, and she was observed off antibiotics. Within 1 month, the musical hallucinations had returned, but they were "tolerable." The improvement in her short-term memory also deteriorated, and she was restarted on oral doxycycline. A SPECT brain scan showed moderately decreased perfusion in the frontoparietal, distal temporal, and prefrontal cortex bilaterally. The musical hallucinations and memory loss have persisted over 4 months. CD57 lymphocyte levels were decreased before treatment and remained below the normal range during oral and IV antibiotic therapy (Fig. 1).

Discussion

Musical hallucinations are four times more common in women than in men, with an average age of onset of 60 years.¹ In the largest review of 46 cases, three quarters of patients had no psychiatric illness and two thirds suffered from deafness.¹ Whereas a gradual onset of hallucinations is associated with deafness, a sudden onset suggests the presence of brain lesions.¹ The type of music is often patriotic or lyrical and may reflect early childhood experiences, as in the case of our patients. The music may be perceived as annoying, intrusive, or pleasing, depending on the psychodynamics of the individual.¹ Various composers, from Beethoven, Schu-

mann, and Donizetti to Brian Wilson of the Beach Boys, have reportedly been affected by these hallucinations.²⁻⁴

There has been controversy over whether musical hallucinations are caused by otologic or cerebral disease.^{2,3,8} These hallucinations have been associated with stroke, epilepsy, brain tumors, alcohol withdrawal, psychotropic medications, and Parkinson's disease,¹⁻⁸ and they have been linked to cortical and midbrain infections, including neurosyphilis.¹⁻⁴ Furthermore, musical hallucinations have been described with pontine lesions and brain abscesses in the absence of deafness.⁶⁻⁸ A recent study attributed these hallucinations to lesions in the right temporal lobe, which contains the auditory

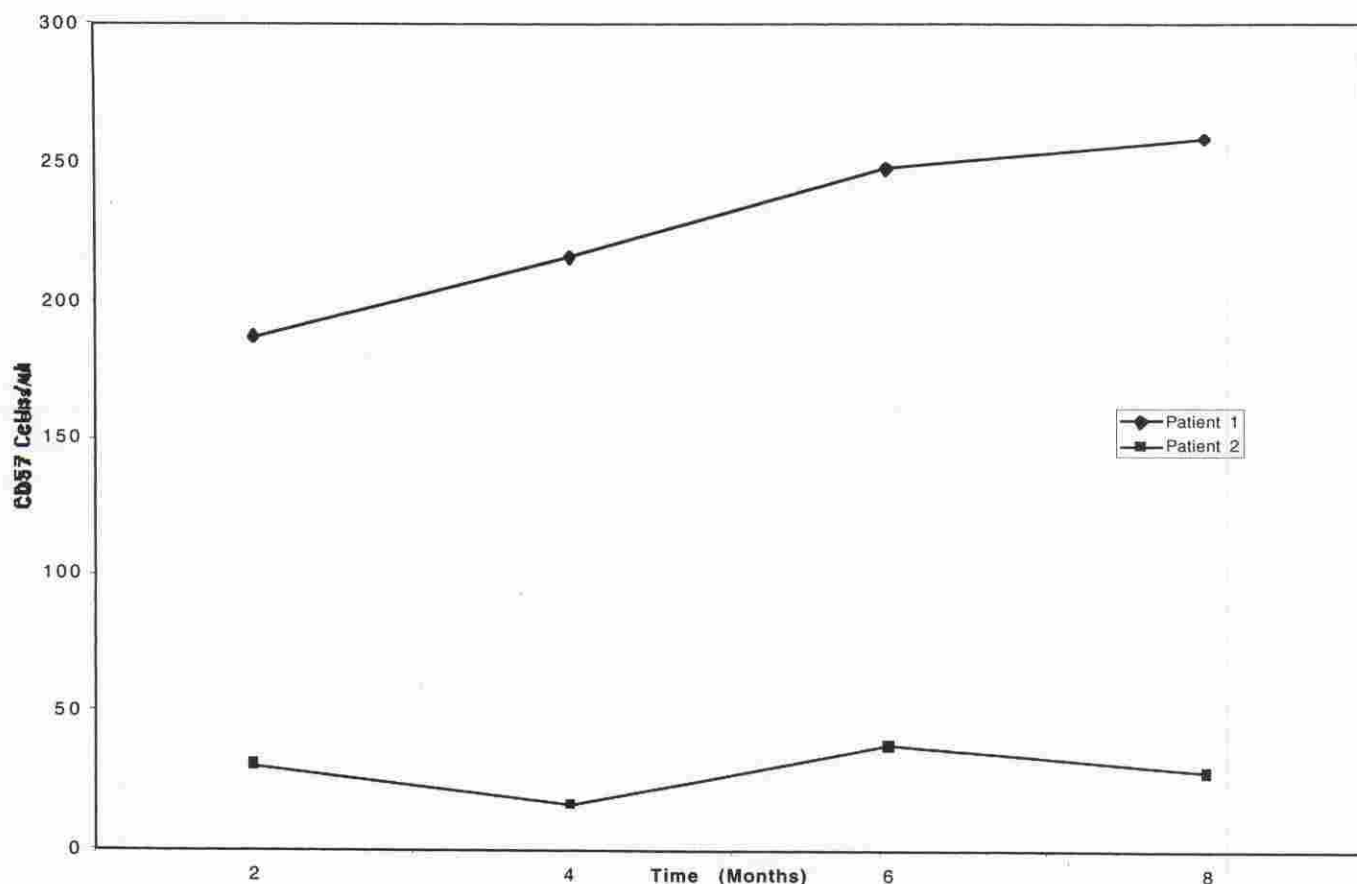


Fig. 1 CD57 lymphocyte subset changes. Normal CD57 lymphocyte range, 60 to 360 cells/ μ l.

association area for nonverbal (eg, musical) stimuli.⁵ Thus, cerebral disease may be responsible for musical hallucinations in certain cases.

Our patients developed musical hallucinations after initiation of oral antibiotic therapy for neurologic Lyme disease (Table 1). Each patient had evidence of active Lyme disease that persisted despite oral antibiotic treatment. Patient 1 had a positive test for *B. burgdorferi* in cerebrospinal fluid after receiving oral antibiotics, and Patient 2 had persistent memory problems that failed to respond to oral doxycycline but improved with IV ceftriaxone. Neither patient had any evidence of hearing impairment, seizure activity, renal dysfunction, or neuropsychiatric illness before the onset of Lyme disease symptoms, and both patients had cerebral lesions documented on MRI scans. In addition, SPECT scanning re-

vealed that Patient 2 had lesions in the right temporal lobe, the area that has been associated with nonverbal (eg, musical) auditory processing.⁵ Thus, there was evidence of persistent spirochetal infection at the time that musical hallucinations supervened in each case, and involvement of the right temporal lobe was documented in one case.

Each patient was on stable doses of medications that have not been associated with musical hallucinations. Although antibiotic therapy could have been responsible for these symptoms, antibiotics have not previously been identified as a cause of musical hallucinations.¹⁻⁸ Furthermore, Patient 1 had received the same antibiotics (clarithromycin and amoxicillin) in the past without any side effects, and her musical hallucinations responded to IV antibiotic therapy. Patient 2 developed musical hallucinations after the onset of

Table 1. Characteristics of patients with musical hallucinations and Lyme disease^a

Patient no.	Age/sex	Lyme disease diagnosis (yr)	Musical hallucination	Brain MRI	Antibiotic treatment
1	66/F	7	"The Star-Spangled Banner"	Positive	Oral, IV
2	80/F	2	Italian opera	Positive	Oral, IV

^aMRI, magnetic resonance imaging; IV, intravenous ceftriaxone.

a Parkinson-like syndrome associated with positive testing for Lyme disease. Of note, the Parkinsonian symptoms resolved with oral doxycycline, but the musical hallucinations did not. However, the musical hallucinations resolved with IV antibiotic therapy and recurred when this treatment was discontinued. Although a causal relationship between Lyme disease and musical hallucinations was not definitively established in our patients, neurologic involvement with the spirochete *B. burgdorferi* appeared to be the most likely cause of these hallucinations. Whether the hallucinations were caused by cortical or brainstem abnormalities remains undetermined, but involvement of the right temporal lobe in Patient 2 suggests that cortical dysfunction was responsible for these symptoms. Musical hallucinations have been noted in several patients with hearing loss and chronic Lyme disease (R.B. Stricker, personal observation), so this auditory symptom may be more common than previously reported.

Lyme disease has been called the new "great imitator" because the protean manifestations of this spirochete-mediated infection are reminiscent of syphilis in the preantibiotic era.¹¹ On the basis of animal and human studies of the disease, evidence of infection may persist for months to years despite appropriate antibiotic therapy.¹²⁻¹⁴ Recently, it has been shown that *B. burgdorferi* can persist in migratory macrophages,^{15,16} explaining penetration of the organism into brain tissue and accounting for resistance to antibiotic therapy in neurologic Lyme disease. With increasing recognition of the disease, novel neurologic and immunologic features have been identified.^{17,18} For example, CD57 lymphocytes comprise a natural killer cell subset that is selectively decreased in untreated patients with chronic Lyme disease.¹⁸ Patient 1 had been treated repeatedly with oral antibiotics over 7 years, and her CD57 lymphocyte level was initially normal (Fig. 1). However, this level increased with IV antibiotic therapy, suggesting that the "normal" range may vary according to the stage of disease in patients with *B. burgdorferi* infection.¹⁸ Patient 2 had decreased CD57 lymphocytes before the onset of musical hallucinations (Fig. 1), and the level remained low despite oral and IV antibiotic therapy. The recurrence of auditory hallucinations and a persistently low CD57 level in this patient support the concept of chronic infection with *B. burgdorferi* and the need for prolonged antibiotic therapy for chronic Lyme disease.¹⁸⁻²¹

In a previous study, we showed that patients with predominant neurologic symptoms of Lyme disease had significantly lower CD57 lymphocyte levels than patients with predominant musculoskeletal symptoms of the disease.¹⁸ In addition to being located on lymphoid cells, the CD57 antigen (also known as Leu-7 or HNK-1) has been found on various central and peripheral nerve cells.²²⁻²⁴ This glycoprotein antigen appears to function as a cell adhesion molecule that promotes cell-cell contact and neurite outgrowth of motor neurons.²² On the basis of a recent study, CD57 may also play a role in immunologic signaling by binding inter-

leukin-6.²⁵ Consequently, a decrease in neuronal expression of this glycoprotein might contribute to neurologic dysfunction and persistent spirochetal infection in the central nervous system. The relationship between immunologic dysfunction and neuropathology in Lyme disease merits further study.

Conclusion

We report the first cases of musical hallucinations associated with neurologic Lyme disease. The documented cerebral lesions in our patients and lack of otologic disease in both cases support the concept that musical hallucinations may result from a central neurologic process rather than an otologic source. IV antibiotic therapy appeared to be effective in treating this striking complication of *B. burgdorferi* infection. Patients who develop musical hallucinations without an obvious cause should be screened for infection with the Lyme disease spirochete.

Acknowledgments

We thank Drs. Brian Fallon, Firoze Jungalwala, Nick Harris, Marilyn Robertson, Lawrence Eng, and Virginia Sherr for helpful discussion. We also are grateful to Drs. Walter Prehn and Michael Powell for patient referrals. We thank Kathleen Dickson, Art Doherty, Phyllis Mervine, Jean Hubbard, Lee Lull, Kathy Kimber, and Billi Goldberg for technical assistance, and David Thomas for manuscript preparation.

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I cannot change the whole world, but I can change a small part of it.

—Kay Florentino

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